

CLAIMS

1. A process for producing an antibody composition using a cell, which comprises using a cell into which a double-stranded RNA comprising an RNA selected from the following (a) or (b) and its complementary RNA is introduced:

(a) an RNA comprising the nucleotide sequence represented by any one of SEQ ID NOs:9 to 30;

(b) an RNA consisting of a nucleotide sequence in which one or several nucleotide(s) is/are deleted, substituted, inserted and/or added in the nucleotide sequence represented by any one of SEQ ID NOs:9 to 30 and having activity of suppressing the function of an enzyme relating to the modification of a sugar chain in which 1-position of fucose is bound to 6-position of N-acetylglucosamine in the reducing end through α -bond in a complex type N-glycoside-linked sugar chain.

2. The process according to claim 1, wherein the enzyme relating to the modification of a sugar chain in which 1-position of fucose is bound to 6-position of N-acetylglucosamine in the reducing end through α -bond in the complex type N-glycoside-linked sugar chain is α 1,6-fucosyltransferase.

3. The process according to claim 2, wherein the α 1,6-fucosyltransferase is a protein encoded by a DNA selected from the group consisting of the following (a) to (h):

(a) a DNA comprising the nucleotide sequence represented by SEQ ID NO:1;

(b) a DNA comprising the nucleotide sequence represented by SEQ ID NO:2;

(c) a DNA comprising the nucleotide sequence represented by SEQ ID NO:3;

(d) a DNA comprising the nucleotide sequence represented by SEQ ID NO:4;

(e) a DNA which hybridizes with a DNA consisting of the nucleotide sequence represented by SEQ ID NO:1 under stringent conditions and encodes a protein having α 1,6-fucosyltransferase activity;

(f) a DNA which hybridizes with a DNA consisting of the nucleotide sequence represented by SEQ ID NO:2 under stringent conditions and encodes a protein having α 1,6-fucosyltransferase activity;

(g) a DNA which hybridizes with a DNA consisting of the nucleotide sequence represented by SEQ ID NO:3 under stringent conditions and encodes a protein having α 1,6-fucosyltransferase activity;

(h) a DNA which hybridizes with a DNA consisting of the nucleotide sequence represented by SEQ ID NO:4 under stringent conditions and encodes a protein having α 1,6-fucosyltransferase activity.

4. The process according to claim 2, wherein the α 1,6-fucosyltransferase is a protein selected from the group consisting of the following (a) to (l):

- (a) a protein comprising the amino acid sequence represented by SEQ ID NO:5;
- (b) a protein comprising the amino acid sequence represented by SEQ ID NO:6;
- (c) a protein comprising the amino acid sequence represented by SEQ ID NO:7;
- (d) a protein comprising the amino acid sequence represented by SEQ ID NO:8;
- (e) a protein consisting of an amino acid sequence in which one or more amino acid(s) is/are deleted, substituted, inserted and/or added in the amino acid sequence represented by SEQ ID NO:5 and having α 1,6-fucosyltransferase activity;
- (f) a protein consisting of an amino acid sequence in which one or more amino acid(s) is/are deleted, substituted, inserted and/or added in the amino acid sequence represented by SEQ ID NO:6 and having α 1,6-fucosyltransferase activity;
- (g) a protein consisting of an amino acid sequence in which one or more amino acid(s) is/are deleted, substituted, inserted and/or added in the amino acid sequence represented by SEQ ID NO:7 and having α 1,6-fucosyltransferase activity;
- (h) a protein consisting of an amino acid sequence in which one or more amino acid(s) is/are deleted, substituted, inserted and/or added in the amino acid sequence represented by SEQ ID NO:8 and having α 1,6-fucosyltransferase activity;
- (i) a protein consisting of an amino acid sequence which has 80% or more homology to the amino acid sequence represented by SEQ ID NO:5 and having α 1,6-fucosyltransferase activity;
- (j) a protein consisting of an amino acid sequence which has 80% or more homology to the amino acid sequence represented by SEQ ID NO:6 and having α 1,6-fucosyltransferase activity;
- (k) a protein consisting of an amino acid sequence which has 80% or more homology to the amino acid sequence represented by SEQ ID NO:7 and having α 1,6-fucosyltransferase activity;
- (l) a protein consisting of an amino acid sequence which has 80% or more homology to the amino acid sequence represented by SEQ ID NO:8 and having α 1,6-fucosyltransferase activity.

5. The process according to any one of claims 1 to 4, wherein the cell into which the RNA having activity of suppressing the function of an enzyme relating to the modification of a sugar chain in which 1-position of fucose is bound to 6-position of N-acetylglucosamine in the reducing end through α -bond in a complex type N-glycoside-linked sugar chain is introduced is a cell which is resistant to a lectin which recognizes a sugar chain structure in which 1-position of fucose is bound to 6-position of N-acetylglucosamine in the reducing end through α -bond in an N-glycoside-linked sugar chain.

6. The process according to claim 5, wherein the cell is resistant to at least one lectin selected from the group consisting of the following (a) to (d):

- (a) a *Lens culinaris* lectin;
- (b) a *Pisum sativum* lectin;
- (c) a *Vicia faba* lectin;
- (d) an *Aleuria aurantia* lectin.

7. The process according to any one of claims 1 to 6, wherein the cell is selected from the group consisting of a yeast cell, an animal cell, an insect cell and a plant cell.

8 The process according to any one of claims 1 to 7, wherein the cell is a cell selected from the group consisting of the following (a) to (i):

- (a) a CHO cell derived from Chinese hamster ovary tissue;
- (b) a rat myeloma cell line YB2/3HL.P2.G11.16Ag.20 cell;
- (c) a mouse myeloma cell line NS0 cell;
- (d) a mouse myeloma cell line SP2/0-Ag14 cell;
- (e) a BHK cell derived from Syrian hamster kidney tissue;
- (f) an antibody-producing hybridoma cell;
- (g) a human leukemia cell line Namalwa cell;
- (h) an embryonic stem cell;
- (i) a fertilized egg cell.

9. The process according to any one of claims 1 to 8, wherein the cell is a transformant into which a gene encoding an antibody molecule is introduced.

10. The process according to claim 9, wherein the antibody molecule is selected from the group consisting of the following (a) to (d):

- (a) a human antibody;
- (b) a humanized antibody;
- (c) an antibody fragment comprising the Fc region of (a) or (b);
- (d) a fusion protein comprising the Fc region of (a) or (b).

11. The process according to claim 9 or 10, wherein the antibody molecule belongs to an IgG class.

12. The process according to any one of claims 1 to 11, wherein the antibody composition is an antibody composition having higher antibody-dependent cell-mediated cytotoxic activity than an antibody composition produced by a parent cell into which a double-stranded RNA comprising an RNA selected from the following (a) or (b) and its complementary RNA is not introduced:

- (a) an RNA comprising the nucleotide sequence represented by any one of SEQ ID NOs:9 to 30;
- (b) an RNA consisting of a nucleotide sequence in which one or several nucleotide(s) is/are deleted, substituted, inserted and/or added in the nucleotide sequence represented by any one of SEQ ID NOs:9 to 30 and having activity of suppressing the function of an enzyme relating to the modification of a sugar chain in which 1-position of fucose is bound to 6-position of N-acetylglucosamine in the reducing end through α -bond in a complex type N-glycoside-linked sugar chain.

13. The process according to claim 12, wherein the antibody composition having higher antibody-dependent cell-mediated cytotoxic activity is an antibody composition which comprises antibody molecules having complex type N-glycoside-linked sugar chains in the Fc region, and in which a ratio of sugar chains in which fucose is not bound to N-acetylglucosamine in the reducing end in the sugar chains among the complex type N-glycoside-linked sugar chains is higher than that of an antibody composition produced by the parent cell.

14. The process according to claim 13, wherein the complex type N-glycoside-linked sugar chains are sugar chains in which 1-position of fucose is not bound to 6-position of N-acetylglucosamine in the reducing end through α -bond in the sugar chains.

15. The process according to any one of claims 12 to 14, wherein the antibody composition having higher antibody-dependent cell-mediated cytotoxic activity is an antibody composition which comprises antibody molecules having complex type N-glycoside-linked sugar chains in the Fc region, and in which the ratio of sugar chains in which fucose is not bound to N-acetylglucosamine in the reducing end in the sugar chains among the complex type N-glycoside-linked sugar chains is 20% or more.

16. The process according to any one of claims 12 to 15, wherein the antibody composition having higher antibody-dependent cell-mediated cytotoxic activity is an antibody composition which comprises antibody molecules having complex type N-glycoside-linked sugar chains in the Fc region, and in which the complex type N-glycoside-linked sugar chains are sugar chains in which fucose is not bound to N-acetylglucosamine in the reducing end.

17. A cell into which an RNA capable of suppressing the function of an enzyme relating to the modification of a sugar chain in which 1-position of fucose is bound to 6-position of N-acetylglucosamine in the reducing end through α -bond in a complex type N-glycoside-linked sugar chain is introduced, and which is used in the process according to any one of claims 1 to 16.

18. The cell according to claim 17, wherein the enzyme relating to the modification of a sugar chain in which 1-position of fucose is bound to 6-position of N-acetylglucosamine in the reducing end through α -bond in a complex type N-glycoside-linked sugar chain is α 1,6-fucosyltransferase.

19. A cell in which an RNA selected from RNAs of the group consisting of the nucleotide sequences represented by any one of SEQ ID NOs:9 to 30 is introduced or expressed.

20. A double-stranded RNA consisting of an RNA selected from the following (a) or (b) and its complementary RNA:

(a) an RNA comprising the nucleotide sequence represented by any one of SEQ ID NOs:9 to 30;

(b) an RNA consisting of a nucleotide sequence in which one or several nucleotide(s) is/are deleted, substituted, inserted and/or added in the nucleotide sequence represented by any one of SEQ ID NOs:9 to 30 and having activity of suppressing the function of an enzyme relating to the modification of a sugar chain in which 1-position of fucose is bound to 6-position of N-acetylglucosamine in the reducing end through α -bond in a complex type N-glycoside-linked sugar chain.

21. A DNA corresponding to the RNA described in claim 20 and a complementary DNA to the DNA.

22. A recombinant DNA which is obtainable by introducing a DNA corresponding to the RNA described in claim 20 and a complementary DNA to the DNA into a vector.

23. The recombinant DNA according to claim 22, which expresses the double-stranded RNA according to claim 20.

24. A transformant which is obtainable by introducing the recombinant DNA according to claim 22 or 23 into a cell.

25. A method for constructing a cell which is resistant to a lectin which recognizes a sugar chain structure in which 1-position of fucose is bound to 6-position of N-acetylglucosamine in the reducing end through α -bond in a complex type N-glycoside-linked sugar chain, which comprises introducing or expressing the double-stranded RNA described in claim 20 in a cell.

26. The method according to claim 25, wherein the cell which is resistant to a lectin which recognizes a sugar chain structure in which 1-position of fucose is bound to 6-position of N-acetylglucosamine in the reducing end through α -bond in a complex type N-glycoside-linked sugar chain is resistant to at least one lectin selected from the group consisting of the following (a) to (d):

- (a) a *Lens culinaris* lectin;
- (b) a *Pisum sativum* lectin;
- (c) a *Vicia faba* lectin;
- (d) an *Aleuria aurantia* lectin.

27. A method for suppressing the function of an enzyme relating to the modification of a sugar chain in which 1-position of fucose is bound to 6-position of N-acetylglucosamine in the reducing end through α -bond in a complex type N-glycoside-linked sugar chain, which comprises using an RNA selected from RNAs of the group consisting of the nucleotide sequences of any one of SEQ ID NOs:9 to 30.

28. The method according to claim 27, wherein the enzyme relating to the modification of a sugar chain in which 1-position of fucose is bound to 6-position of N-acetylglucosamine in the reducing end through α -bond in a complex type N-glycoside-linked sugar chain is α 1,6-fucosyltransferase.